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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/322,067	05/27/1999	JEFFREY SKOLNICK	10886/047001	7470

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EXAMINER

BORIN, MICHAEL L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 06/17/2002

25

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/322,067

Applicant(s)

Skolnick et al

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jul 16, 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-14, 16-20, 22, and 44-60 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-14, 16-20, 22, and 44-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other. _____

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/9/02 has been entered.

Status of Claims

2. Claims 2-14, 16-20,22, 44-60 are pending.

Specification

3. The disclosure is repeatedly objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See, pages 4,5,8,46,83,97,100,101,122-124,126,128,136,137,141. Applicant is requested to delete the embedded hyperlink and/or other form of browser-executable code.

It is noted that applicant defers correction of the issue until the time the allowed subject matter is identified.

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Claim Rejections - 35 USC § 112, second paragraph.

4. Claims 2-14, 16-20,22, 44-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons:

The base claims 45,53,54 recite that geometric constraints are to be selected between at least three atoms, which means that there may be more than three atoms selected. The criteria for selection of atoms in the latter case is not clear. The description of the third atom in the claims is different the first two. Consequently, for the embodiments wherein more than three atoms are selected, it is not clear whether the atoms should be as defined for the first/second atom, or as for third atom. Clarification is requested.

Claim Rejections - 35 USC § 101

5. Claims 16-20,22 remain rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The rejection is maintained for the instant claims for reasons of record.

Claims 16-20,22 are drawn to a "functional site descriptor" and libraries of said descriptors. The product as claimed is not a process, machine, manufacture, or composition of matter. "Functional descriptive material" consisting of data

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structures is nonstatutory when claimed as descriptive material *per se*. MPEP 2106, section "1. Nonstatutory subject matter".

6. Claims 53,2-14, 16-19,20,2245-52 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to "a computer program product in a computer readable medium", wherein the claimed product is merely a descriptive material comprising a set of geometric constraints (such as a set of distances, angles, etc.) together with the information on identity of one amino acid residue. The invention as a whole is directed to a mere program listing, i.e., it is a descriptive material *per se*. As a descriptive material that cannot exhibit any functional interrelationship with the way in which computer processes are performed, the claimed subject matter does not constitute a statutory process. The descriptive material claimed alone does not impart functionality of either to the data as so structured or to the computer.

Claim Rejections - 35 USC § 102 and 103.

7. Claim 2-14, 16-20,22, 44-60 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C.103(a) as obvious over Wallace et al.

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The claims as amended are drawn to a computer program product (and computer system containing said product) comprising description of one amino acid and geometric constraints between at least three different atoms located at three different residues. One of these atoms must be a backbone atom. The "geometric constraints" are defined in the specification (p. 19) as relative coordinates, or distances, or angles.

Wallace reference, as discussed in preceding Office actions, teaches method of searching protein structural databases for functional sites. In particular, the reference explores 3D coordinate templates for sites comprising a Ser-His-Asp triad. The method of Wallace identifies an amino acid residue (i.e., as step (a) of claim 53) and relative positions between atoms of three residues, Ser, His, and Asp, and, optionally, other atoms. The residues are considered to be interacting when the distance between the atoms of the three residues (i.e., the same as "geometric constraints" in step (b) of claim 53) is less than van der Waals radius plus 1 Å. The distance can be measured between any atoms of the residues; however, the preferred embodiment of the method includes defining distance from functional oxygens of Asp and Ser to His residue. Note, that the reference does not limit distances between side chain atoms; the distance is measured between Asp and Ser residues (functional oxygens of their side chain in the preferred embodiment) and His residue for which the location of set point is not specified and thus can be either a side chain ring or

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a backbone atom (see, for example, discussion of relative position of Ser214 towards "the backbone of His", p. 1008, line 8). The flow diagram of method of implementing calculations of 3D template is given on Fig. 1. Further the method is applicable to, using applicant's terminology, "functional site descriptors" comprising not only the catalytic Ser-His-Asp triad but also atoms of different amino acid residues. See section "The catalytic tetrad" on pages 1007-1009.

It is the Examiners position that all the elements of Applicant's invention with respect to the specified claims are instantly disclosed by the teaching of the reference cited above. It is noted that the Wallace reference, although using a computer database Protein Data Bank, does not specifically mention usage of a computer to implement the described method of searching structural databases. It is Examiner's position that the amount of data analyzed is such that it necessitates the use of a computer; therefore the method used in Wallace is regarded as a computer implemented method, and its result - as a computer program product.

However, should it appear unobvious that Wallace et al use a computer, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to implement method of Wallace using a computer to facilitate computation of huge amount of data.

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In regard to claims 20-22 drawn to a library containing functional site descriptors, the generated output from database searches are always placed in a separate output file.

Response to argument

Applicants argue that claims as amended require that at least one of the atoms must be a backbone atom, which is not described in Wallace. First, the reference teaches that distances are measured between Asp and Ser residues (functional oxygens of their side chain in the preferred embodiment) and His residue for which the location of set point is not specified and thus can be either a side chain ring or a backbone atom (see, for example, discussion of relative position of Ser214 towards "the backbone of His", p. 1008, line 8). Second, the Wallace method is not limited to the preferred embodiment describing particular residues of particular enzyme. Further, applicant argues that nothing in Wallace suggests that a functional site descriptor can be represented by non-catalytic backbone atoms. However, the instant claims are not drawn to "catalytic" or "non-catalytic" atoms; all the claims require is that atoms belong to different residues.

8. Claims 2-14, 16-20,22, 44-60 remain rejected under 35 U.S.C. 102(b) as anticipated by Holm et al. The rejection is maintained for the reasons of record set forth earlier for claims 1,3-10,12,15-22,43-50.

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Response to arguments

Applicant argues that Holm does not teach a functional site descriptors. However, the instant specification defines "functional site" as any site in protein that has a function. Such broad definition encompasses an entire protein as well. The focus of the reference is on the definition and prediction of the functional site descriptors, for example, the amino acid residues present in an enzymatic active site, such as in urease.

Prior art made of record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

9. US 6251620 teaches method for determining a three-dimensional structure of a ZAP-70 containing SH2 domain comprising utilizing coordinates of specified atoms (including backbone atoms) having a defined distance limitation from a backbone atom.

10. US 5978740 teaches a computer-implemented method of modeling binding pocket of a protein comprising defining residues present in the binding pocket and defining distances from backbone atoms.

11. US 5241470 teaches method for determining three-dimensional structure of peptides (including 3-D structure of their functional sites) comprising imposing steric

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limitations to positions of backbone atoms by defining optimal steric positions with minimum steric interaction energy.

Conclusion.

12. No claims are allowed.

13. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June 13, 2002

mlb

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

